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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,746	10/14/2003	Reid M. Rubsamen	AERX-080CIP2	6142

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/685,746	RUBSAMEN ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 19-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/07/06 has been entered.

Receipt is acknowledged of the Amendments and Remarks filed on 11/07/06. Claims 1, 7 and 19 have been amended and new claims 20-26 have been added (claim 24 has not been indicated as NEW in the claim set).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite for failing to recite a proper Markush type claim. A proper language in a Markush claim includes the statement "selected from the group consisting of". Remaining claims are rejected for depending on a rejected base claim.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 5, 7-13, 19-23 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drug Facts and Comparisons in view of Butrous et al (EP 1097711).

Drug Facts and Comparisons discloses that sildenafil citrate has been approved for and is being use for both pulmonary arterial hypertension and erectile dysfunction. It is disclosed that to treat erectile dysfunction doses of 50 mg are recommended. However the dose may be taken up to 100 mg or reduced to 25 mg, as needed. The sildenafil citrate is taken from 4 hours to 30 minutes before sexual activity. The reference lacks disclosure on inhalation as the route of administration.

Butrous et al teaches the use of certain **cGMP PDE5 inhibitors**, including in particular the compound **sildenafil** for the treatment of pulmonary hypertension (see abstract). Butrous also discloses that the International Patent application WO94/28902 the compound of sildenafil was found effective in treating male erectile dysfunction (see [0002]). It is also disclosed that the said compounds can be administered by **inhalation**. Inhaled formulations have advantages in delivering the active compound directly to the lung area, producing a **faster effect** than orally delivered formulations. The suitable

particle size for the said aerosol is between 0.5 and 5 microns. The aerosol formulations are conveniently generated from a **pressurized container**, pump, spray or nebulizer with the use of a suitable **propellant**. For such delivery **single-dose sprays, multi-dose metered nebulizers, inhalers or atomizers can be used** (see [0023]).

Butrous also discloses that the said compounds can be administered together with **other active agents** such as nifedipine, diltiazem, ilprost, adenosine, nitric oxide, etc (see [0036]). The said formulations are said to be either in solution form (see [0025], [0035] and example 4) or in a micronised powder formulation and delivered by a **dry powder inhalation device** (see [0032] and example 3).

Drug Facts and comparisons discloses a method of treating erectile dysfunction and a method of treating pulmonary arterial hypertension by administering formulations comprising sildenafil citrate. Butrous et al discloses aerosolized formulations comprising sildenafil citrate and devices suitable for the administration. Butrous et al also teaches the pulmonary administration of the said sildenafil citrate for treating pulmonary hypertension. However it would have been obvious to one of ordinary skill in the art to have dispensed the disclosed aerosolized sildenafil citrate of Butrous et al for treating erectile dysfunction as well because it is disclosed by Butrous et al and known in the art that pulmonary route provides for a locally acting and faster onset of the drug.

Claims 2-4, 6 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drug Facts and Comparison in view of Butrous et al (EP 1 097 711) as applied to claims 1, 5, 7-13 and 19-23 and 25-26 above, and further in view of Blood et al (6,579,968).

The combined references above, while disclosing the addition of other agents to the aerosol formulations of sildenafil, lack specific disclosure on adding testosterone.

Blood et al teach compositions and methods for treating sexual dysfunction. The compositions are suggested for male sexual dysfunction such as erectile dysfunction, and female sexual dysfunction (see abstract). Blood et al also discloses that men who have low levels of testosterone benefit form treatments with testosterone injections or pills. Testosterone propionate has also been employed to increase or augment female libido (col. 1, line 52 to col. 2, line 9). Blood et al also teaches administration of the formulations through inhalation and by using inhalation devices (see col. 7, line 62 to col. 8, line 65).

It would have been obvious to one of ordinary skill in the art to have modified the formulations and methods of the combined references on treating erectile dysfunction with sildenafail citrate by including an additional agent such as testosterone to provide more benefits to patients, men or women, who need these therapies. In other words Butrous et al teach that other active agents can be added to the formulations of

sildenafil and Blood et al teaches that testosterone has been effective in treating sexual dysfunctions in men and women. Thus one of ordinary skill in the art would have been motivated to use a combinatorial therapy in order to provide a more effective treatment for those in need of such treatments.

Response to Arguments

Applicant's arguments with respect to claims 1-19 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mina Haghighatian
Patent Examiner
Art Unit 1616
December 21, 2006